REMARKS

I. Status of the Application

This paper responds to a Final Office Action mailed December 1, 2006. The present application was originally filed with claims 1-15. Following a first Office action, mailed September 13, 2004, Applicant amended claims 1-3, 5-10, and 13-15. In response to a final Office action, mailed February 28, 2005, Applicant filed an RCE which included an after final amendment that modified claim 14, canceled claim 15 without prejudice or disclaimer, and added claim 16. Following an Office action mailed June 21, 2005, Applicant amended claims 1, 2, 6, 7, 9, 10-12, 14 and 16, and added new claim 17. A final Office action mailed December 9, 2005 rejected claims 1-14, 16 and 17, and in response, Applicant filed an RCE which amended claim 16, canceled claim 17 without prejudice or disclaimer, and added new claim 18. Following a non-final Office action mailed June 21, 2006, Applicant amended claims 1, 6, 9-14, and 18, canceled claim 16, and added new claim 19. The present paper amends claims 1, 12-14, 18, and 19 and cancels claims 4 and 6-11 without prejudice or disclaimer. Therefore, claims 1-3, 5, 12-14, 18, and 19 are currently under consideration in the application. Applicant respectfully submits that entry of this after-final amendment is proper because it places the claims in condition for allowance.

II. Amendment of Claims 1, 12-14, 18, and 19

Applicant has amended independent claim 1 to recite a composition having a pH of about 6.5 to about 7.0 and has amended claims 12-14, 18, and 19 to delete redundant subject matter, eliminate references to canceled claims, or both. Applicant submits that these amendments are fully supported in the application as originally filed. For example, support for the pH range can be found in Table 1 at page 12 and in original claims 1, 4, 8, and 14.

III. Election/Restriction

The Office has withdrawn claim 19 under 37 CFR § 1.142(b) as being "independent or distinct from the invention originally claimed" since it is a "method of

treatment claim whereas the originally claimed invention was drawn to compositions." Applicant respectfully requests reinstatement of method of treatment claim 19 because, as noted in the prior response, claim 19 recites the same method of treatment recited in claim 16, which was previously examined and not subject to a restriction requirement. Applicant added claim 19 only after the Office objected to multiple-dependent claim 16 under 37 CFR § 1.75(c) for improperly depending on a higher-numbered claim.

IV. Rejection of claims 1-14 and 18 Under 35 U.S.C. § 103

The Office rejected claims 1-14 and 18 under 35 U.S.C. § 103 as being unpatentable over WO 99/58573 in view of Zour et al. According to the Office action, the "'573 reference discloses solid and liquid pharmaceutical compositions comprising gabapentin analogs with increased stability" and includes "amino acids that are disclosed as agents capable of inhibiting lactam formation." The Office action notes that the '573 reference discloses "[s]weetening agents, such as mannitol and xylitol" which "may also be added to the compositions 'if needed'." The Office action further states that "Zour et al. disclose stability studies of gabapentin in aqueous solutions" which "demonstrates that the stability of gabapentin in aqueous solution is greatest at a pH of 6.0, and at 45 °C gabapentin demonstrated minimal degradation when formulated at a pH from 5.5 to 7.0." According to the Office action, the "Examiner has not made a 35 U.S.C. 102 rejection (anticipation) because the WO '573 reference does not disclose the pH of the solutions."

Applicant respectfully submits that all of the pending claims are patentable over WO 99/59573 and Zour et al. As an initial matter, Applicant submits that WO 99/58573 cannot anticipate the claims of the present invention because, in addition to failing to recite the pH limitation, WO 99/58573 does not describe pharmaceutical compositions in which "one or more polyhydric alcohols comprises about 25 g to about 75 g per 100 mL of the composition."

Furthermore, Applicant submits that the combination of WO 99/58573 and Zour et al. do not render the claims *prima facie* obvious, because modifying the '573 reference as suggested by the Office action would change the principle of operation of the reference. *See* MPEP § 2143.01(VI) (8th ed., Rev. 5) ("If the proposed modification or

combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious."). As noted in the application, Applicant has discovered that gabapentin or pregabalin can be formulated in a stable liquid pharmaceutical composition having low levels of lactam when the pH of the composition is about 5.5 to about 7.0 and when the composition includes one or more polyhydric alcohols. See Specification, page 4, lines 4-7, and page 9, lines 7-9. Moreover, the stable formulation is achieved without the inclusion of an additional amino acid, such as glycine. *See, e.g.*, claims 1, 6, 9 and 10, above. As noted in the Office action, WO 99/59573 requires the presence of an additional amino acid to inhibit lactam formation, and therefore its absence would change the principle of operation of the reference.

Applicant also submits that WO 99/58573 and Zour et al. do not render the claims *prima facie* obvious because there is no motivation to include a polyhydric alcohol in the pharmaceutical composition. Indeed, WO 99/59573 teaches away from inclusion of a polyhydric alcohol in pharmaceutical compositions containing gabapentin or pregabalin without concomitant use of an additional amino acid to stabilize the formulation. For instance, Example 2 in WO 99/59573 shows that the addition of a polyhydric alcohol (xylitol, sample "e") to an aqueous gabapentin solution increases lactam formation (compare sample "d" and sample "e" in Table 4). In contrast, the addition of glycine (sample "f") to an aqueous solution of gabapentin and xylitol decreases lactam formation (compare sample "f" with samples "d" and "e" in Table 4). The stability of the claimed formulations in the absence of an amino acid besides gabapentin or pregabalin is itself an indicia of unobviousness. *See* MPEP § 2144.04(II.B) (8th ed., Rev. 5) ("Omission of an element with retention of the element's function is an indicia of unobviousness.").

Applicant further submits that the claimed pH range and the use of one or more polyhydric alcohols in the claimed amounts result in pharmaceutical compositions having surprising and unexpected chemical stability. To support this conclusion, Applicant submitted in its response of April 7, 2006, a declaration under 37 CFR § 1.132, which described data that showed the influence of pH and the presence of a polyhydric alcohol

on lactam formation. The data indicated that aqueous compositions containing gabapentin exhibited improved stability when formulated at a pH of about 5.5 to about 7.0. Moreover, aqueous gabapentin formulations formulated at a pH of about 6.5 to about 7.0 and containing a polyhydric alcohol exhibited improved stability over formulations that did not. *See* Applicant's Response of April 7, 2006 at pages 7-8 and Declaration Under 37 CFR § 1.132. This latter result is completely unexpected and renders the claims patentable.

In view of the above, Applicant submits that the pending claims are patentable over WO 99/58573 and Zour et al., and respectfully requests withdrawal of the rejection.

V. Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are patentable over the prior art of record. If the Examiner has any questions, Applicant requests that the Examiner telephone the undersigned.

Applicant submits that no fees are due in connection with the filing of this paper. However, if Applicant has overlooked any required fees, please charge the fees to deposit account number 16-1445.

Respectfully submitted,

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